



Ministry of Health
National Pharmaceutical Regulatory Agency

SUPPLEMENTARY DOCUMENTS FOR GCP INSPECTION

GUIDANCE FOR INDUSTRY

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Control

This document is issued as a supplementary reference to the Malaysia Guideline for GCP Inspection, 3rd Edition.

It is not legally binding and will be periodically revised to reflect changes in regulatory requirements and advancements in the clinical trial environment.



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APPENDIX A: EXAMPLES OF CRITICAL FINDINGS

General

- Use of a prohibited substance(s) without having received prior authorisation.

Prohibition

- Clinical Trial Import Licence (CTIL) and/or Clinical Trial Exemption (CTX) is not obtained, as required in accordance with the *Controls of Drugs and Cosmetics Regulation 1984* and *Malaysian Guideline for Application of Clinical Trial Import Licence and Clinical Trial Exemption* in Malaysia.

Application for Authorisation

- Misrepresentation or falsification of data submitted to obtain authorisation to conduct clinical trials.

Authorisation

- Continuing a clinical trial after authorisation has been suspended or cancelled.
- Importation of an investigational product when authorisation is suspended or cancelled.

Amendment

- Submission of falsified, misleading, or deceptive information in an application for amendment.
- Failure to notify NPRA following the implication of an amendment, where the clinical trial endangered the health of the trial participant or another person.
- Failure to halt a clinical trial during suspension or cancellation.

Good Clinical Practices

- Evidence of fraud such as “fabricating” participants or falsification of study data.

Records

- Sponsor withholding data (e.g. for purpose of deception).
- Failure to report SUSARs which occurred inside and/or outside Malaysia.
- No records relating to the use of an investigational product in a clinical trial.
- No records relating to the enrolment of clinical trial participants.
- No record to demonstrate the sponsor's oversight and responsibility, particularly with respect to the management of Service Providers.

Additional Information and Sample(s)

- Providing false, misleading or deceptive investigational product sample(s) or additional information relevant to the investigational product or the clinical trial.

Computerised System

- Insufficient validation of the electronic data capture (EDC) system to demonstrate accuracy, reliability, and consistent performance for its intended use, posing a risk to the integrity of clinical trial data.
- Absence of secure user access controls, leading to unauthorised access or manipulation of clinical trial data.
- Failure to maintain audit trails that are complete, secure, and tamper-proof, preventing tracking of data creation, modification, or deletion.
- Inability to retrieve or reproduce original electronic records and associated metadata.

APPENDIX B: EXAMPLES OF MAJOR FINDINGS

Interpretation

- Voting members of the Independent Ethics Committee (IEC)/ Institutional Review Board (IRB) were not independent of the qualified investigator and/or the sponsor of the clinical trial.
- Approvals of clinical trials without a quorum of members with the required representation.
- Major changes to previously approved protocols that increased health risks to participants, were given expedited approval only.

Application for Authorisation/CTIL/CTX

- Information contained in the application was incomplete or incorrect.

Authorisation/CTIL/CTX

- Failure to disclose all Malaysian clinical trial sites for clinical trial that require CTIL/CTX or which require notification to NPRA.
- Failure to provide all necessary information, not previously provided in the application, prior to the importation of an investigational product at a clinical trial site.

Notification

- Failure to notify NPRA when changes are made to the chemistry and manufacturing information or to the approved protocol.

Amendment

- Implementation of an amendment without obtaining authorization from IEC/IRB.
- Failure to implement IEC/IRB approved amendment at a clinical trial site.

Good Clinical Practices

- Approved investigators lack the qualifications required to conduct the clinical trial.

- Medical care and trial-related decisions not under the supervision of the qualified investigator.
- Failure to obtain IEC/IRB approval of the protocol and/or the informed consent forms prior to trial initiation.
- Protocol(s) and/or informed consent form(s) not updated, and/or participants not re-consented when new information becomes available regarding health and safety concerns, or use of the investigational product which endanger the health of the clinical trial participant or another person.
- Failure to obtain IEC/IRB approval prior to implementation of amendments to protocol or informed consent forms.
- Informed consent not obtained from participants before enrolment into the trial or after major amendments to the informed consent form.
- Informed consent forms not administered properly or forms not signed and dated.
- Inadequate source data to substantiate clinical trial results.
- Clinical trial was not conducted in accordance with the approved protocol.
- Sponsor did not notify the qualified investigator of SUSARs that occurred at other sites.
- Qualified investigators failed to notify the sponsor and/or IEC/IRB of SUSARs in a timely manner.
- No procedures in place for reporting of new safety information to the qualified investigators.
- Significant clinical endpoint data not collected on time, not correctly recorded, or not accurately transcribed/transferred to case report forms.
- Inadequate systems in place for investigational product(s) accountability.
- Inadequate storage or monitoring or handling controls in place for investigational product(s)
- Source data was not verified for quality, completeness and integrity.
- System(s) and/ or procedure(s) that assure the quality of every aspect of the clinical trial were not implemented.
- The informed consent forms did not contain all of the required information.
- Inadequate monitoring of the clinical trial site by the sponsor.

- Personnel involved in the conduct of the clinical trial are not qualified by education, training and experience to assume responsibility for the proper conduct of trial.
- Incomplete documentation of protocol deviations.
- Lack of documentation that the sponsor was informed of the protocol deviations.

Records

- No security procedures in place for electronic records or electronic signatures.
- The electronic data system was not validated.
- Sponsor has no or incomplete records of all adverse events which occurred inside or outside of Malaysia.
- Incomplete records pertaining to the enrolment of trial participants.
- Incomplete records pertaining to the shipment, receipt, handling, storage, dispensing, return or destruction of the investigational product.
- Quantities of investigational product not accounted for through the various stages of shipment, receipt, disposition, return or destruction of the lots of the investigational product.
- Signed and dated qualified investigator undertakings were not available for each trial site prior to the commencement of the investigator's responsibilities.
- Copies of the protocol/amendments and informed consent forms approved by the IEC/IRB are not retained for each clinical trial site.
- Absence of IEC/IRB attestation for each clinical trial site stating that it has reviewed and approved the protocol, the informed consent forms and that it functions in compliance with GCP.
- No audit trails in electronic records showing activities, including initial data entries and subsequent changes to data fields or records, by whom, when and, where applicable, why the changes were made.
- No provisions for retention of trial records as required by the Malaysian Guidelines for Good Clinical Practice.
- Incomplete records pertaining to the use of a drugs in a clinical trial.
- The subject ID was handwritten on the ECG printout, the date and time of the ECG were manually altered on the printout.

- The original ECG printout consist of trial participant name and identification number, the site personnel manual blackout the information to conceal the trial participant personal information.
- There was no access control on the usage of the ECG.

Suspected Unexpected Serious Adverse Reactions (SUSARs) Reporting

- Sponsor failed to report SUSARs to NPRA.
- Sponsor did not comply with the reporting timeline for SUSARs.
- Sponsor failed to submit, within the prescribed timeline, an assessment of the importance and implication of any findings made.

Early Trial Termination/Temporary Halt of a Clinical Trial

- Sponsor did not notify NPRA of the temporary halt or early termination of the clinical trial, whether in its entirety or at a trial site, within fifteen (15) working days from the date of the temporary halt or early termination.
- Sponsor did not provide NPRA with the reasons for the temporary halt or early termination, nor the potential impact on the proposed or ongoing clinical trials.
- Sponsor did not inform all qualified investigator(s) of the temporary halt or early termination of the trial, including the reasons for such actions, or did not provide this information in writing.
- Sponsor did not suspend the importation of the investigational products as of the date of the temporary halt or early termination.
- Following termination of the clinical trial, the Sponsor resumed importation of the investigational product without submitting the required information to NPRA.
- The clinical trial continued at one or more sites despite the Sponsor having stated that the trial was temporary halted or early terminated at those sites.

Sponsor Oversight and Responsibility

- There was no clear Quality Management System framework within the Sponsor's clinical operations to demonstrate adequate oversight of the clinical trial in accordance with GCP requirements.

APPENDIX C: EXAMPLES OF MINOR FINDINGS

Application for Authorisation/CTIL/CTX

- Sponsor did not retained copies of previous versions of the investigator's brochures pertaining to the investigational product(s).

Good Clinical Practices

- Incomplete delegation of responsibilities and/or incomplete signature log.
- Correction of data not initialed and/or dated.
- Minor errors in transcribing of data from source documents to case report forms.
- Investigational product(s) was not manufactured, handled or stored in accordance with the applicable Good Manufacturing Practice requirements.
- Source data were stored in an unsecured location.

Labelling

- The labelling of the investigational product(s) did not comply with the requirements outlined in the *Controls of Drugs and Cosmetics Regulation 1984* and *Malaysian Guideline for Application of Clinical Trial Import Licence and Clinical Trial Exemption*.

APPENDIX I: CONDUCT OF INSPECTION AT INVESTIGATOR SITE

1.0 LEGAL AND ADMINISTRATIVE ASPECTS

1.1 Communication with NPRA

- Approval from National Medical Research Register (NMRR)
- Approval of CTIL/CTX
- Submission of variation application(s)
- Notification of protocol amendment(s)
- Notification of IB amendment(s)
- Submission of other relevant notification(s), if applicable
- Reporting of SUSARs
- Submission of Interim reports
- Notifications of protocol deviation
- Submission of study summary report
- Submission of final CSR
- Notification of premature termination or suspension of a trial, if applicable

1.2 Communication with IEC/IRB

- Documented and dated approval/favourable opinion from IEC/IRB for the conduct of trial (approval was made with adequate composition)
- Approval of the protocol and amendment(s)
- Approval of the informed consent form and amendment(s)
- Approval of the IB and amendment(s)
- Approval of CRF templates and/or subject diaries, including amendment(s)
- Approval of advertisement materials and/or subject handouts
- Notification of protocol deviation
- Submission of interim report
- Submission of final CSR
- Reporting of SAEs and SUSARs
- Notification of premature termination or suspension of a trial, if applicable

1.3 Contract(s) and Agreement(s)

- Date of signed Clinical Trial Agreement (CTA) and/or Confidentiality Agreement

1.4 Clinical Trial Insurance Documentation

- Initial and updated version and communication to IEC/IRB
- Validity period of the Clinical Trial Insurance must cover duration of the study.

2.0 ORGANISATIONAL ASPECTS

2.1 Implementation of the Trial at the Site

- Agreements between the sponsor or sponsor's representatives and the investigator
- Qualifications by education, training, and experiences for the investigator's team—including external staff provided by the service providers—in the relevant clinical areas. Trainings should include detailed instructions on the protocol, investigational products, and their assigned trial-related activities. All personnel assisting in the trial must receive trial-related trainings to enable them to fulfil their delegated responsibilities beyond their usual training and experience.
- A record should be maintained to document the delegation of trial-related activities by the investigator. The documentation should be proportionate to the significance of the trial-related activities. In situations where such activities are performed as part of routine clinical practice, formal delegation documentation may not be required.
- Compatibility of the workload of the investigator(s) and the staff with the requirements of the study
- Organisation of the site for the study (organisation chart, specific training, specific equipment, specific procedures)
- Compliance with the planned time schedule for the study

- Correct implementation of the correct versions of the protocol and its amendments
- Documentation demonstrating that, despite sponsor support in identifying potential service providers, the investigator retains the final decision regarding the suitability of the service providers and provides supervision over all delegated activities.
- Agreement between the investigator/institution with service providers for trial-related activities.
- Documentation of all protocol deviations, including those communicated to the investigator by the sponsor. For important deviations, evidences must be provided that the investigator has explained the deviation and implemented appropriate measures to prevent recurrence, where applicable.

2.2 Facilities and Equipment

The aim is to verify the proper use, adequacy and validation status of procedures and equipment used during the performance of the trial. The inspection may include a review of the following:

- Facilities:
 - Their suitability for the protocol requirements and the characteristics of the study being inspected.
 - Where appropriate, the inspection may also cover to facilities outside of investigator sites (i.e. Central Image Reading Facilities)
- Records demonstrating fitness for purpose (e.g. maintenance and calibration) for equipment used for important trial activities.
- Documentation of the assessment of fitness for purpose for non-trial-specific computerised systems used in the trial (e.g., clinical practice computerised systems).

2.3 Management of Biological Samples

The aim is to examine, conditions and documentation regarding the management of biological samples, if applicable:

- Collection: person in charge of this task, dates and handling procedures.
- Handling and storage of the biological samples before processing, analysis or shipping.
- Shipping conditions of the biological samples.

2.4 Organisation of the Documentation

To determine whether general documentation, in accordance with the Malaysian Guidelines for GCP and applicable regulatory requirements, is available, dated and signed, and where applicable, how it is archived at the trial site.

- Documentation defining what constitutes source record(s) for the trial, including methods of data capture and their location, as established prior to trial initiation, and any updates made to the definition during the course of the trial.
- Documentation confirming that the investigator had timely access to all relevant data, including data from external sources (e.g. central laboratory data, central imaging data, other institution's records, and where applicable, electronic patient reported outcome (ePRO) data) that could impact participant's eligibility, treatment or safety.
- Records to demonstrate that the investigators conducted timely reviews of such data to ensure participant's safety and protocol compliance.
- Trial records as specified in ICH E6(R3) Appendix C (Essential Records for the Conduct of a Clinical Trial).
- Documentation to confirm that the investigator/institution retained all essential records for the required retention period.

2.5 Monitoring and Auditing

The following points will be examined:

- Documentation of Sponsor/Sponsor's representatives monitoring and follow-up activities, including the number, scope, and dates of site visits; content of monitoring visit reports; actions required by the monitor; and the monitoring visit log.
- Monitoring plan/SOPs.
- Audit certificates – if available (from sponsor file)

2.6 Use of Computerised Systems

Where computerised systems are used for the trial, their validation status should be verified. Such systems may be study-specific and provided by the Sponsor (e.g. eCRFs, electronic patient diaries, IVRS) or site-specific systems routinely used at the trial site (e.g. electronic medical records, online laboratory data systems, ECG systems).

- Documentation confirming that the investigator/institution has implemented appropriate measures to protect trial data and information maintained or retained within their systems from unauthorized access, disclosure, dissemination, alteration, inappropriate destruction, or accidental loss, including safeguards such as access controls, regular data backups, and data integrity checks, in compliance with the applicable regulatory requirements.
- Documentation demonstrating that trial-specific computerised systems were validated, and that non-trial-specific systems were assessed and deemed fit for their intended purposes in the trial.
- Documentation demonstrating that the investigator received appropriate instructions from the Sponsor on the use of computerised systems, including navigation of systems, access to trial data, and review of relevant metadata for trial participants under their responsibilities.

3.0 INFORMED CONSENT OF TRIAL PARTICIPANTS

To determine whether informed consent was obtained in accordance with GCP guidelines from an appropriate sample of participants (including those whose medical records were reviewed), or the their legally acceptable representative, and, where applicable, by an impartial witness, prior to the enrolment in the study. This review must include all participants whose medical records were examined.

- Initial and any subsequent re-consent forms, as used and approved by the IEC/IRB, are signed and dated by both the participant and the person conducting the informed consent discussion (physical or electronic signature).
- Information sheet versions were approved by the IEC/IRB, includes all the elements required by the Malaysian Guidelines for GCP and current regulations.
- Participant, or their legally acceptable representative were provided with a copy (paper or electronic) of the signed and dated informed consent form and related materials, including any revised versions during the trial.
- Consent was obtained for access to medical records by the regulatory authorities.
- Documentation that the participant or their legally acceptable representatives was informed in a timely manner of any new information affecting willingness to continue participation.
- Assessment records demonstrate whether re-consent was required, considering trial stage and relevance to participants.
- Revised consent materials clearly identify new information, especially emerging safety issues, and were approved by IEC/IRB prior to use.
- Information provided does not contain language that causes the participant or their legally acceptable representatives to waive legal rights or release the investigator, institution, Sponsor, or service providers from liability for negligence.
- Impartial witness signature and date are contemporaneous with the participant/legally acceptable representative, where applicable.

- Age-appropriate assent information provided and assent obtained prior to enrolment. Procedures in place for obtaining consent if the minor reaches the legal age during the trial.
- Documented procedures for exceptional circumstances in accordance with applicable regulations.
- Informed consent approaches used to provide information to participants (e.g. text, images, videos, or other interactive tools), should be carefully considered for their suitability. When computerised systems are used, trial participants should be given the option to use a paper-based method as an alternative. Remote consent may also be used where appropriate, in accordance with the applicable regulatory requirements.

4.0 REVIEW OF THE TRIAL PARTICIPANT DATA

To determine whether the investigator and site personnel conducted the clinical trial in accordance with the approved protocol and its amendments through source data verification.

- Evaluate the source records for organisation, completeness, and legibility.
- Any corrections to data recorded in the CRF are made in accordance to the Malaysia GCP Guideline and applicable regulatory requirements.

4.1 Characteristics of Participants included in the Trial

To determine whether participants were enrolled in the trial in accordance with the approved protocol, and where applicable, any protocol deviations or violations related to enrolment were appropriately documented and addressed, and described in the clinical study report.

- Documentation and interviews demonstrating that the investigator had adequate capability and resources, based on retrospective or current recruitment data, to recruit the proposed number of eligible participants within the recruitment period agreed with the Sponsor.
- Documentation relating to participant screening, eligibility assessment (inclusion and exclusion criteria), enrolment, and withdrawal or discontinuation

was available, where applicable. Supporting source records demonstrate fulfilment of all inclusion criteria and confirm that no exclusion criteria specified in the protocol were present.

- Where applicable, records of discussions between the investigator or site personnel and the participant or their legally acceptable representative regarding withdrawal or discontinuation were available and demonstrate that such discussions were conducted to understand the reason(s) for withdrawal and to explore potential options, without exerting undue influence on the participant's decision to refuse or withdraw from the trial.

4.2 Participants' Visits Calendar

To determine whether participant visits were conducted in accordance with the visit schedule specified in the approved protocol. This includes a review of visit dates to verify that trial visits were performed within the protocol-defined timelines.

4.3 Efficacy and safety assessment data

To verify whether efficacy and safety data recorded in the CRF are consistent with the corresponding source data generated during the trial and whether adequate data management procedures were implemented. Where applicable, all data related to trial endpoints should be compared with source documents.

- All adverse event (AEs) and serious adverse events (SAEs) documented in the clinical study report are complete and consistent with the data recorded in the CRFs.
- Medical records will be reviewed as source data to identify any AEs that may not have been captured in the CRFs. Where electronic medical records are used, the inspectors should be granted appropriate access for source data review.
- Review of AEs and SAEs reporting timelines to confirm compliance with applicable regulatory requirements.

- Verification that, where applicable, the investigator had informed participants of the trial results and the treatment received following unblinding, in accordance with the information provided by the Sponsor.
 - All adverse events (AEs) and serious adverse events (SAEs) reported in
- This check will also include whether adverse events recorded in the site records are also recorded in the CRF and were reported to the sponsor, IEC/IRB and authorities in accordance with current regulations.

4.4 Concomitant Therapy and Intercurrent Illness

To verify whether concomitant therapies and intercurrent illnesses were managed in accordance with the protocol and appropriately documented in the CRF and source records.

5.0 MANAGEMENT OF THE INVESTIGATIONAL PRODUCT(S) (IPs) AND ACCOUNTABILITY

To verify whether all the activities related to the investigational product(s) were handled and managed in accordance with the approved protocol.

- Verification that the investigator/institution retained overall responsibility for IPs accountability throughout the trial.
- Review of instructions for handling IPs and trial-related materials, where not included in the approved protocol or Investigator's Brochure.
- Documentation of IPs receipt, inventory, storage, dispensing to participants, return to the Sponsor, and destruction or alternative disposition of unused IPs.
- Documentation of treatment allocation and randomization, including dates, quantities, batch/serial numbers, expiry dates (where applicable), and unique codes assigned to investigational products and trial participants.
- Verification that participants received IPs and doses in accordance with the approved protocol, as supported by the IP accountability records.
- Assessment on treatment compliance.
- Documentation of any unblinding events, including reason for unblinding (e.g. accidental unblinding, emergency unblinding for participant safety, or

unblinding related to a SAE).

- Verification on IP-related records were completed by authorized personnel in accordance with the site SOP's and applicable requirements.
- Assessment of the suitability of IPs storage conditions and areas; and review of corresponding temperature monitoring records.
- Review of pharmacy- or institution-specific SOPs governing IP management, where applicable.
- Verification that access to IPs were controlled from receipt through dispensing and return or destruction.
- Verification that IPs labelling complied with the applicable regulatory requirements

APPENDIX II: CONDUCT OF INSPECTION ON COMPUTERISED SYSTEM

The main points to consider:

- **General Principles**

In general, the following key process should address the full data life cycle with focus on the criticality of the data and it should be implemented proportionately and documented appropriately:

- a) Processes to ensure the protection of the confidentiality of trial participant's data.
- b) Processes for managing computerised systems to ensure that they are fit for purpose and used appropriately.
- c) Processes to safeguard essential elements of the clinical trial, such as randomisation, dose adjustments and blinding.
- d) Processes to support key decision making, such as data finalisation prior to analysis, unblinding, allocation to analysis data sets, changes in clinical trial design and, where applicable, the activities of, for example, an IDMC.
- e) The responsibilities of the sponsor, investigator and the activities of other parties with respect to a computerised system used in clinical should be clear and documented.

- **Procedures for the use of Computerised System**

A clear documented procedure should be in place to ensure appropriate use of the computerised system in clinical trials for essential activities related to data collections, handling and management.

- **Training**

The responsible party should ensure that personnel using the computerised system are appropriately trained in their use.

- **Security**

- The security of the trial data and records should be managed throughout the data life cycle.
- The security controls implemented should include user management and ongoing measures to prevent, detect and/or mitigate security breaches.
- The responsible party should maintain adequate backup of the data.
- Procedures shall be established to cover the system security measures, data backup and disaster recovery to ensure that unauthorised access and data loss are prevented. Such measures should be periodically tested, as appropriate.

- **Validation**

- The responsible party is responsible for the validation status of the system throughout its life cycle. The approach to the validation of the computerised system should be based on a risk assessment that consider the intended use of the system.
- System should be validated prior to use and subsequent changes to the system should be in line with the change control procedures.
- A procedure review may be appropriate to ensure the computerised system remain in a validated state throughout the life cycle of the system.
- Both standard system functionality and protocol-specific configurations and customisation should be validated. Interfaces between the system should also be defined and validated.
- Validation should demonstrate the system conforms to the requirements for completeness, accuracy and reliability and its performance is consistent with its intended purpose.
- The responsible party should ensure that the computerised system are validated as fit for purpose for use in the trial, including those developed by other parties, and the validation documentation is maintained and retained.

- **System Release**

The trial-specific system which include the updates resulting from protocol amendments should only be implemented, release or activated for individual investigator sites after all necessary approval for the clinical trial relevant to that investigator site have been received.

- **System Failure**

Contingency procedures should be in place to prevent loss or lack of accessibility to data essential to participant safety, trial decision or trial outcomes.

- **Technical Support**

Where appropriate, there should be a procedure in place to document, evaluate and manage issues with the computerised systems and a periodic review to the cumulative issues is recommended. Based on the criticality of the issued, it should be resolved in a timely manner

- **User Management**

- Procedures should be in place to ensure that user access permission are appropriately assigned based on a user's duties and functions, blinding arrangement and the organisation to which users belong.
- Access permission should be revoked when they are no longer needed and a process should be in place to ensure access and assigned roles and permission are periodically reviewed, where relevant.
- Authorised user and access should be clearly documented, maintained and retained. These records should include any updates to a user's roles, access permissions and time of access permission being granted.

The following guidelines shall be used as references for inspection on Computerised Systems:

- PIC/S Guidance on Good Practices for Computerised Systems in Regulated “GXP” Environments (PI 011-3). The hyperlink to the PIC/S site is <http://www.picscheme.org/index.php>
- Reflection paper on expectations for electronic source data and data transcribed to electronic data collection tools in clinical trials, EMA, 2010
- Code of Federal Regulations. Title 21-Food and Drugs; Part 11: Electronic Records; Electronic Signatures.
<http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCFR/CFRSearch.cfm?CFRPart=11&showFR=1>
- Guidance on GxP data integrity, MHRA, 9 March 2018
- Guideline on Computerised System and Electronic Data in Clinical Trial (EMA/INS/GCP/112288/2023), 9 March 2023.
- Conducting Clinical Trial with Decentralized Elements Guidance for Industry, Investigators and Other interested parties, USFDA, September 2024.

APPENDIX III: CONDUCT OF INSPECTION AT SPONSOR SITE AND/OR SERVICE PROVIDERS SUCH AS CONTRACT RESEARCH ORGANISATION (CRO)

SPONSOR OR SERVICE PROVIDERS QUALITY SYSTEM INSPECTION

The purpose of this inspection is to evaluate the quality assurance and quality control systems established by the Sponsor or service provider(s) to ensure that clinical trials are conducted, and that data are generated, recorded, and reported in compliance with the protocol, Good Clinical Practice (GCP), and applicable regulatory requirements.

This inspection also aims to verify whether the trial has been conducted, and data were generated, documented, and reported in compliance with the approved protocol, GCP principles, and Sponsor procedures. Procedures and requirements applicable at the time of the trial will be considered and, where relevant, compared with those in place at the time of the inspection. Additionally, specific clinical trial inspections may be conducted to address questions outlined in a request for a GCP inspection.

The following items may be reviewed during a Sponsor and/or service providers inspection; however, this list is not exhaustive:

1.0 Organisation and Personnel

The aim is to evaluate if the sponsor/service provider has a well-established organisation for clinical research activities and has a sufficient number of properly qualified and trained personnel for each area.

Review may include:

- Organisational charts that identify the key personnel in each area
- The independence of the Quality Assurance Unit.
- The job description, qualification and training of the individuals involved at any stage of the clinical trial process.

2.0 Facilities and Equipment

To identify and evaluate the facilities used for archiving or storage of investigational medicinal product(s), as well as the equipment employed. Particular attention will be given to computerised systems (hardware, software, communications, etc.) to assess their validation status and suitability for their intended purposes. Documented procedures should be in place to ensure the appropriate use of computerised system in clinical trials, covering essential activities related to data collection, handling and management.

3.0 Sponsor or Service Provider(s) Standard Operating Procedures

Procedures will be reviewed, as applicable, to verify their compliance with GCP standards and applicable regulatory requirements.

4.0 Sponsor Audit and Quality Assurance System

The aim is to assess whether the Sponsor (and/or its contracted service providers, where applicable) has established and implemented an effective quality assurance and audit system that is fit for purpose, risk-based, and proportionate to the complexity and risks of the clinical trials, to ensure compliance with the protocol, GCP, and applicable regulatory requirements.

Determined if the procedures include:

- Establishment and maintenance of a documented quality assurance system covering clinical trial activities
- Risk-based planning and conduct of audits independent from routine monitoring and quality control.
- Audits of key clinical trial processes, including monitoring, data management, safety reporting, clinical study report preparation, archiving, and computerised system validation.
- Audits of contracted service providers, subcontractors, and vendors involved in trial-related activities.

Key aspects subject to review include evidence that the Sponsor has (this list is not exhaustive):

- Established documented SOPs governing the audit and quality assurance programme, including audit planning, conduct (on-site and/or remote), reporting, and follow-up.
- Risk-based audit programme and/or audit plan, guided by factors such as trial complexity, participant risk, critical trial processes, and identified issues.
- Appointed auditors who are independent of the activities being audited and qualified by appropriate training and experience.
- Maintained documentation of audit activities, including audit plans, audit trails, observations, and findings.
- Implemented procedures for addressing audit observations through corrective and preventive actions (CAPA), including tracking, verification of effectiveness, and prevention of recurrence.
- Established procedures for the identification, escalation, and management of serious and/or persistent non-compliance with GCP or regulatory requirements.
- Demonstrated appropriate sponsor oversight of outsourced activities through audits and quality assurance activities of contractors and subcontractors.
- Maintained records supporting the integrity, traceability, and confidentiality of audit documentation.

5.0 Implementation and Termination of the Clinical Trial

To review the procedures established for the implementation and termination of the clinical trial. Trial-specific documents will be reviewed for:

- Distribution of sponsor's duties or functions.
- Document preparation (format and content and distribution of protocol, protocol amendments, informed consent documents, investigator brochure, CRF and any other trial documents)
- Investigators selection and protocol-related training.
- Agreements between Sponsor and investigators

- Regulatory compliance (obtaining IEC/IRB approval/favourable opinion and necessary authorisations, providing notifications and reports as required by GCP and local regulations)

6.0 Delegation, Outsourcing and Oversight of Trial-Related Duties

The aim is to verify that the Sponsor has established and implemented documented procedures for the delegation, transfer, and oversight of trial-related duties to service providers (e.g. CROs) and other third parties.

Determine whether procedures include:

- Risk-based pre-selection, qualification, and ongoing assessment of service providers and subcontractors.
- Clear documentation of delegated trial-related duties, including scope of responsibilities and effective dates.
- Contracting processes, including handling and documentation of contract amendments.
- Oversight mechanisms for outsourced and subcontracted activities.

Key aspects subject to review (this list is not exhaustive):

- Established and maintained written agreements with investigators/institutions, service providers, and other trial-related committees (e.g. IDMC, adjudication committees), clearly defining roles, responsibilities, and reporting arrangements.
- Assessed the suitability and capability of service providers prior to selection to ensure they can adequately perform transferred trial-related activities.
- Implemented appropriate oversight of important trial-related activities transferred to service providers, including activities further subcontracted.
- Ensured service providers have implemented appropriate quality management systems for their assigned trial-related activities and have procedures for timely reporting of incidents that may impact participant safety or data reliability.
- Maintained documentation supporting the sponsor's consideration of inputs from relevant stakeholders, including healthcare professionals and patients, during trial

design and development of participant-facing materials, in accordance with ICH E8(R1).

- Obtained and maintained documentation confirming the identity, organisation, and GCP compliance of the relevant IRB/IEC, including official declarations or statements where applicable.
- Established trial-specific criteria for the identification and classification of important protocol deviations.
- Established processes for the timely identification, escalation, assessment, and resolution of issues arising during trial conduct, with documented communication, impact assessment, and follow-up actions.
- Established and operated trial oversight committees, where applicable (e.g. IDMC, endpoint adjudication committees), with documented charters, defined membership and expertise, conflict of interest management, and records of recommendations and decisions.
- Maintained documentation related to the identification, management, and follow-up of noncompliance, including records of corrective and preventive actions.
- Maintained documentation related to insurance, indemnification, and compensation arrangements for the clinical trial.

7.0 Monitoring

The aim is to assess whether the Sponsor has established and implemented an effective monitoring system that is fit for purpose, risk-based, and proportionate to the complexity and risks of the clinical trials, ensuring protection of participants and reliability of trial results.

Key aspects subject to review include evidence that the Sponsor has (this list is not exhaustive):

- Established documented monitoring SOPs and a trial-specific monitoring plan, defining monitoring approach/strategy, frequency, and scope, including activities conducted in decentralised settings.

- Implemented risk-based monitoring, supported by documented risk assessments and proportionate risk control measures, with periodic review and adjustment.
 - Documentation related to risk management, including records of risk identification across clinical trial processes, evaluation of potential risks based on likelihood, detectability, and impact. Risks should be considered across the processes and systems, including computerised systems, used in the clinical trial.
 - Impact, implementation of risk proportionate risk control measures within protocol design, monitoring plans, agreements, SOP adherence, and training.
 - Communication of identified risks and mitigation activities to relevant stakeholders.
- Conducted monitoring in accordance with the monitoring plan and maintained timely monitoring reports, sponsor/CRO oversight, and documented follow-up actions.
- Ensured monitors and relevant trial personnel are appropriately qualified, trained, and documented, including those involved in centralised monitoring activities.
- Ensured direct access to source records for authorised sponsor representatives and regulatory authorities, in compliance with data protection and confidentiality requirements.
- Applied appropriate monitoring methods, including source data review/verification, centralised monitoring, data analytics, and on-site or remote visits, with risk-based sample selection where applicable.
- Established processes for issues and deviations management, including escalation, impact assessment, targeted remediation, and prevention of recurrence. Important quality issues or important deviations, and the corrective actions taken should be documented in the clinical trial report. Ensured compliance with data protection, confidentiality, and data security requirements, supported by appropriate documentation.

8.0 Investigational Medicinal Product(s)

The assess whether the Sponsor has established and implemented procedures for handling and management of investigational medicinal product in accordance with the current GMP, GCP and applicable regulations.

Key aspects subject to review include (this list is not exhaustive):

- GMP-compliant manufacturing, packaging, labelling, and quality control of IMPs.
- End-to-end IMP supply chain management, including shipment, receipt, storage, accountability, return, recall, and destruction, with full traceability.
- Randomisation, blinding, and code management procedures, including controls to prevent inappropriate unblinding and mechanisms for emergency unblinding without compromising overall trial blinding.
 - Processes to blind sponsor staff, investigators, and trial participants as appropriate to prevent and detect inappropriate unblinding.
 - Procedures allowing rapid emergency unblinding for a participant when medically necessary, while maintaining blinding for other participants.
 - Mechanisms to maintain trial blinding when unblinding occurs for safety reporting to regulatory authorities or IRB/IEC, as appropriate.
- Stability and shelf-life controls, ensuring IMPs are used within approved conditions and expiry.
- Documented systems for retrieval and final disposition of unused, expired, or defective IMPs.

9.0 Sample Management

The procedures established for handling **biological samples** obtained in clinical trials should be reviewed.

10.0 Safety and Adverse Events Reporting

The aim is to assess whether the Sponsor has established and implemented procedures for timely review, management, and communication of safety information, including timely

reporting of serious adverse events and other safety findings to the participants, investigators, IEC/IRB and regulatory authorities, as applicable.

Determine whether procedures include:

- Expedited reporting of adverse drug reactions to regulatory authority(ies), investigators and IEC/IRB, where applicable.
- Timely notification of serious adverse events by investigators.
- Assessment, follow-up, and management of SAEs reported by investigators.
- Preparation, review, and communication of safety updates and periodic safety reports.
- Use of validated computerised systems in support of safety data collection, processing, and reporting.

Key aspects subject to review include (this list is not exhaustive):

- Established documented procedures for systematic review of safety information, including periodic aggregation and assessment of relevant safety data, and for updating the protocol, Investigator's Brochure, informed consent materials, and related documents where necessary.
- Reviewed emerging safety information to assess its impact on participant safety, willingness to continue participation, trial conduct, and regulatory or ethics approval, with timely communication of significant findings to participants, investigators, ethics committees, and regulatory authorities, as applicable.
- Documented assessments of the expectedness of adverse reactions based on applicable product information (e.g. reference safety information in the IB or alternative documents).
- Ensured that urgent safety issues requiring immediate attention or action were identified, assessed, and reported without delay to relevant regulatory authorities, ethics committees, and investigators.
- Implemented processes to promptly identify and manage immediate hazards to participants, including documented actions taken to mitigate risks and protect participant safety.

- Ensured that computerised systems used for safety reporting and safety data management are validated, fit for intended use, and operated in accordance with applicable data protection, confidentiality, and data security requirements.

11.0 Data Handling and Clinical Trial Report

The aim is to evaluate the system established by the Sponsor/CRO for the handling, processing, analysis, and reporting of clinical trial data in the clinical trial report in compliance with protocol, GCP, and applicable regulatory requirements.

Determine if the procedures establish:

Data handling, processing, and analysis procedures, including quality control measures. Preparation and review of the clinical trial report in accordance with ICH standards. Validation, management, and oversight of computerised systems used in the trial. Use and maintenance of audit trails for both paper-based and electronic systems. Key aspects subject to review include (this list is not exhaustive):

- Data handling and quality control:
 - Established and applied quality control measures at appropriate stages of data handling to ensure data accuracy, completeness, consistency, and reliability, with a focus on critical data and relevant metadata.
 - Provided documented guidance to investigators, institutions, and service providers on expectations for data capture, data modification, data retention, and data disposal.
 - Ensured investigators had timely access to trial data collected in accordance with the protocol, including relevant data from external sources, to support decisions related to participant eligibility, treatment, continued participation, and safety.
 - Implemented appropriate measures to manage data that could potentially unblind investigators.
- Data management and traceability:
 - Documented data management activities to be completed prior to data analysis, including processes specific to interim analyses, data reviews by

- oversight committees, and final analyses.
- Established processes to ensure traceability of data processing steps, transformations, and derivations throughout the data lifecycle.
 - Computerised systems and data security:
 - Maintained records for all computerised systems used in the clinical trial, including system purpose, functionality, interfaces, validation status, and assigned responsibilities.
 - Implemented appropriate system controls, including access management, audit trails, data backup, disaster recovery, and IT security measures to protect data integrity and confidentiality.
 - Maintained records of authorised system users, including defined roles and access privileges.
 - Assessed systems used by investigators or institutions that contain source records (e.g., electronic health records) for fitness for purpose, with documented mitigation of any identified limitations.
 - Established procedures requiring investigators and service providers to report system defects, incidents, or failures that could impact trial conduct, participant safety, or data integrity.
 - Statistical analysis:
 - Implemented documented quality control measures for statistical programming and data analysis, including sample size calculations, analysis results for IDMC review, outputs for clinical trial report, statistical or centralized monitoring.
 - Ensured that inclusion or exclusion of trial participants from analysis sets was predefined, justified, and documented in the protocol or statistical analysis plan.
 - Maintained records demonstrating that statistical outputs were traceable to validated statistical programs, properly version-controlled, dated, and protected against unauthorised modification.
 - Clinical trial report:
 - Established procedures for the preparation, review, approval, and

finalisation of the clinical trial report, including documented quality control and formal sign-off by authorised individuals.

12.0 Documentation Archiving

The aim is to assess whether the Sponsor/CRO has established and implemented a system that ensures clinical trial documentation is properly archived, complete, secure, and retrievable for the required retention period in accordance with applicable GCP requirements and local regulations.

Determine if procedures include:

- System for archiving, indexing, and retrieval of trial documents.
- Controlled and authorized access to the archived documents.
- Protection of archived documents from loss, damages, deterioration, or unauthorized access.
- Retention schedules consistent with regulatory and GCP requirements.
- Procedures for transfer of documents in case of site closure or relocation.

Key aspects subject to review include (this list is not exhaustive):

- Established documented procedures for archiving and retrieval of essential trial documents, including regulatory submissions, CRFs, source records, monitoring reports, and trial master files.
- Maintained controlled access to archives with clear assignment of responsibility for custodianship.
- Ensured the physical or electronic storage environment maintains document integrity, confidentiality, and readability throughout the retention period.
- Implemented procedures for secure transfer or retrieval of documents when required, including contingency plans for disaster recovery or site closure.